IGRT to particle therapy. Proton therapy offers dosimetric advantages not possible with x-rays but with a relative biologic effectiveness quite close to photons. Thus, normal tissue tolerances can rely on 100 years of laboratory and clinical experiences. Well-established indications for proton therapy include ocular melanomas, cancer in children, brain tumors, sarcomas and chordomas at the base of the skull and carcinoma of the prostate. There are many opportunities for proton therapy with concurrent chemotherapy to improve the therapeutic ratio compared with x-irradiation. There is considerable potential to increase doses in tumors without increasing toxicity for common diseases such as cancer of the lung. The value of proton therapy is just beginning to be recognized.

Interest in proton therapy has increased dramatically around the world. Japan alone has six clinical proton therapy centers. Four hospital-based proton centers are treating patients in the United States and several others are being planned. The beneficial results of 3D over 2D RT, and of IMRT over 3DCRT contribute to a compelling case for proton beam therapy. As proton therapy equipment becomes less costly and smaller and results of proton therapy are published, one can envision a robust role for proton beam therapy in the future of cancer treatment.

MTP21-01 NSCLC Therapy: How much and how long? Thur, Sept 6, 07:00 - 08:00

Advanced NSCLC chemotherapy: how much and how long?

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Systemic therapy improves survival and quality of life for patients with advanced stage non-small cell lung cancer (NSCLC). It became clear that infact a ëchemotherapy efficacy plateauí had been reached when comparison of multiple two-drug combinations failed to show any benefit of one over another. The role of prolonged or maintenance therapy beyond 3-6 cycles was challenged by the results from two large randomized phase III studies, but there was an apparent flaw as majority of the patients randomized to longer duration of chemotherapy did not receive the planned number of cycles, leading to discontinuation either due to toxicity or disease progression. Therefore, one could only conclude that continuation of combination chemotherapy (two or three drugs) beyond 4 cycles is not a feasible option. A number of new therapeutic options have subsequently emerged during recent times for advanced NSCLC incorporating novel cytotoxic agents (taxanes, gemcitabine, pemetrexed) and targeted agents (erlotinib, bevacizumab). Efforts to improve the outcome for front-line therapy of advanced and metastatic NSCLC have primarily focused on the addition of molecularly targeted agents to platinum-based two drug regimens. Bevacizumab, an antibody against the vascular endothelial growth factor, is the first drug to demonstrate improvement in outcome when added to systemic chemotherapy in advanced disease. Since bevacizumab was given as monotherapy following initial response or disease stabilization on ECOG 4599, it is now used in the maintenance setting for advanced NSCLC. This has led to new insight and a glimmer of hope debate for the role of maintenance therapy in advanced NSCLC, provided it is not associated with any significant long term adverse effects. Both cytotoxic single agents and molecularly targeted agents are suited for evaluation in the maintenance setting. Promising results have been noted with single agent paclitaxel as maintenance therapy following 4 cycles of combination therapy with carboplatin and paclitaxel. Phase III studies are now underway to evaluate the role of single agents such as gemcitabine, pemetrexed and erlotinib(figures 1-3) as maintenance therapy for patients who experience a response or disease stabilization following 4 cycles of combination chemotherapy. Whether this approach will be successful in extending the survival of a select group of patients remains to be seen. It does, in fact, takes maximal advantage of either known active agents in this disease or novel agents which have shown early evidence of provocative activity.

In addition to the evaluation of newer agents to improve the outcome for advanced NSCLC, maintenance therapy represents a novel strategy to increase the therapeutic potential of currently available agents and commonly used regimens. Multiple lines of evidence from recent observations suggest that maintenance therapy with well tolerated chemotherapeutic or targeted agents may benefit patients with advanced NSCLC. This also has the potential to improve the toxicity profile of overall treatment as combination chemotherapy would then be limited to 4 cycles and maintenance therapy would be essentially without any significant adverse effects if chosen optimally. Since maintenance therapy utilizes currently available agents, it may also be associated with better cost-benefit ratio. In the next 1-2 years, the results from several ongoing trials that focus on maintenance therapy will be available. It is hoped that the data will usher in a new treatment paradigm for patients with advanced stage NSCLC.

Figure 1: Maintenance Gemcitabine for NSCLC Phase III Trial (B9E-US-S194) Schema

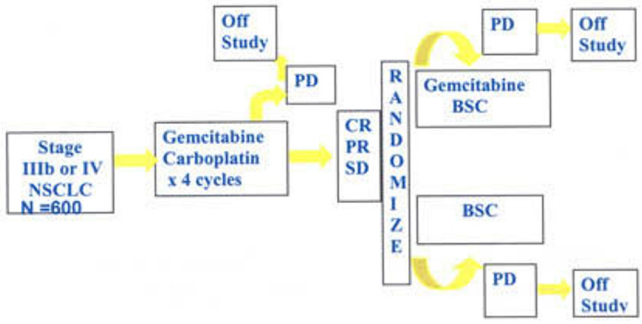

Figure 2: Phase III Trial of Maintenance Pemetrexed for Advanced NSCLC; Schema